

65. (New) A fragment of said splice variant of human telomerase protein according to claim 18.

66. (New) The fragment according to claim 65, wherein said fragment is from 10 to 100 amino acids long.

### REMARKS

Upon entry of the foregoing amendment, claims 16, 18, 19, 22, 65 and 66 are pending in the application. Support for new claims 65 and 66 are found in originally filed claims 19 and 22.

Applicants thank the Examiner for the withdrawal of the rejections under 35 U.S.C. § 112, second paragraph.

#### *Claim Rejections Under 35 U.S.C. § 112, First Paragraph*

The rejection of claims 19 and 22 under 35 U.S.C. § 112, first paragraph, is respectfully traversed. The Examiner alleges that claim 19, which is directed to the fragment of the splice variant of human telomerase protein of claim 16, lacks the written description of a structure. However, the specification provides disclosure of 128 splice variants of human telomerase with different mRNA sequences (see page 22, lines 1-10 and Table 1 and Figure 11). This disclosure provides adequate written description for these splice variants and fragments of these variants are supported on page 3, lines 21-26, in the original claims and in the disclosed sequences. Additionally, the specification provides a variety of assays to determine telomerase activity. In view of the disclosure in the original specification and claims, it is requested that this rejection be withdrawn.

The rejection of claim 18 under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification is respectfully traversed. Specifically, in response to the assertion that the amino acid sequence SEQ ID NO:46 is not encoded by the polynucleotide sequence of SEQ ID NO:45 because the 18<sup>th</sup> codon of the respective encoding DNA sequences is TAC, which encodes the amino acid tyrosine, applicants submit as Appendix A the Declaration of Andrzej Kilian executed on January 2, 2003 ("Declaration"). As the Declaration states, the error in SEQ ID No:46 and

other listed sequences arose because of a clerical error in converting the three letter amino acid code to the one letter amino acid code when preparing the figures for the application. The substitute sequence listing submitted herewith correct the clerical errors in the originally filed sequence listing. In this regard, applicants also enclose red lined copies of drawings that need to be corrected to change the 18<sup>th</sup> amino acid from threonine (T) to tyrosine (Y). In view of the explanation and Dr. Kilian's declaration, it is requested that this rejection be withdrawn.

Claims 16, 19 and 22 under 35 U.S.C. § 112, first paragraph are rejected as being enabling for the variant of human telomerase described by SEQ ID NO:46 and its fragments that may be encoded by the introns, but allegedly not reasonably enabled for any splice variant of human telomerase, its fragments or fragments that are 10-100 amino acids in length is respectfully traversed.

The M.P.E.P. § 2164.01 states that the test for enablement is whether the disclosure at the time of filing contained sufficient information regarding the subject matter of the claims as to enable one skilled in the art to make and use the claimed invention. The standard for determining whether the specification meets the enablement requirement is whether experimentation needed to practice the invention is undue or unreasonable. There are several factors which are considered when determining whether experimentation is "undue."

Experimentation, if any, necessary to practice the full range of the present claims (e.g., claim 16, which is directed to an isolated protein comprising a splice variant of human telomerase) would not be undue. For example, there is considerable direction and guidance in the specification regarding determining the sequences of the splice variants. Specifically, the specification provides the sequences of many, if not all, of the species encompassed by this claim. As noted above, see Table 1 on page 22, which discloses 16 splice variants of telomerase and notes that an independent assortment of known intron sequences would lead to 128 different mRNA sequences. Moreover, the claim is not unreasonably broad because, as defined by the specification, a splice variant of human telomerase protein is a genus of finite number, and Applicants have disclosed a very large number of species of that genus as noted above in Table 1. Additionally, there are several working examples describing the

identification and isolation of the human telomerase gene, characterization of the telomerase gene, and the identification of alternative splicing patterns of telomerase mRNA.

Accordingly, reconsideration and withdrawal of the rejection are respectfully requested.

***Claim Rejections Under 35 U.S.C. § 102(e)***

The rejection of claims 16, 18, 19 and 22 under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,166,178, issued December 26, 2000 ("Cech") is traversed. Applicants respectfully disagree with the Examiner's assertion that Cech discloses a human telomerase splice variant, delta-182 variant, having amino acid sequence SEQ ID NO:5 that is encoded by SEQ ID NO:4. The Examiner suggests that Cech discloses that the delta-182 "may play a biological role in nature (e.g. in regulation of telomerase expression) and find use as therapeutics (e.g. as dominant-negative products that inhibit function of wild-type proteins)."

Cech does not teach that the delta-182 is a splice variant of telomerase. The delta-182 "variant" could easily be, for example, incompletely processed mRNA, and it is submitted that the Examiner is improperly concluding that Cech discloses as splice variant. Accordingly, the reference does not anticipate the claimed invention because Cech does not explicitly or inherently disclose all of the claim elements. The disclosure is certainly not explicit because Cech does not teach or suggest that delta-182 is a splice variant of telomerase. The disclosure also is not inherent because the natural and invariable practice of the reference does not necessarily and inherently meet all of the elements of the claims. The variant, delta-182, is not inevitably and invariably a splice variant of telomerase, and therefore, does not anticipate the claimed invention.

Additionally, applicants submit that the disclosure of the delta-182 variant in Cech is only entitled to a priority date of August 14, 1997, the filing date of one of the parent applications, U.S. Serial No. 08/911,312, and does not have support earlier than this date. Applicants own priority date to which the claims of the present application are entitled predates this August 14, 1997 date, and therefore, the Cech patent and its disclosure of the

delta-182 is not prior art to the pending claims. Thus, for all of the reasons above, Cech does not anticipate the pending claims, and it is requested that it be withdrawn.

Regarding the Examiner's assertion that SEQ ID NO:613 (actually SEQ ID NO:611 is the sequence contained in the Examiner's sequence search) of Cech comprises an amino acid sequence that is 98.7% identical to SEQ ID NO:46, Applicants submit that SEQ ID NO:611, is not a splice variant of human telomerase protein but rather is identified as a "full length hTRT" in Cech in the text preceding the sequence. Additionally, the Examiner has failed to show that Cech has support for this sequence prior to the priority date of the pending claims. For all of these reasons, it is requested that this rejection of claim 18 be withdrawn.

### ***Conclusion***

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Respectfully submitted,

Date: January 21, 2003

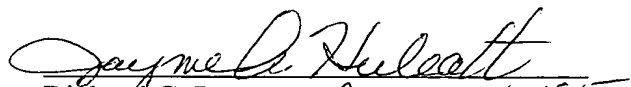
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